

Asymmetric [1,2]-Wittig Rearrangement and Synthesis of Fused Heteroaromatics



Biography

Andrew Harper carried out his undergraduate degree at the University of St Andrews, carrying out research projects under the supervision of Prof. John Walton, Prof. Andrew Smith, and Dr Alan Aitken. In 2013, he started a PhD in the Aitken group.

Institution

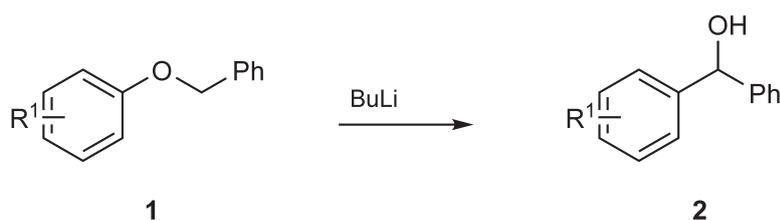
University of St Andrews

Abstract

Science of Synthesis Online has been used to identify methods of performing asymmetric [1,2]-Wittig rearrangement reactions. Procedures for the synthesis of benzyl ethers and *O*-aryl carbamates allowed suitable [1,2]-Wittig rearrangement precursors to be prepared and the chapter on benzo[*b*]furans provided a comprehensive overview of their synthesis.

Discussion

In recent research, the [1,2]-Wittig rearrangement of substituted aryl benzyl ethers **1** to secondary alcohols **2** has been investigated (Scheme 1). As an extension to this methodology, it was of interest to develop an asymmetric variant of this reaction. A text search of *Science of Synthesis* Online for “asymmetric Wittig rearrangement” provided a link to Section 8.1.34.1.7 (Enantioselective Deprotonation Followed by Wittig Rearrangement) which contained examples of enantioselective and diastereoselective [1,2]-Wittig rearrangements of benzylic ethers.

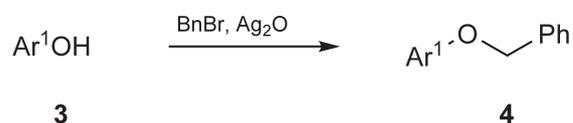


Scheme 1 [1,2]-Wittig Rearrangements of Benzylic Ethers

In the synthesis of one of the target precursors, it was necessary to convert the phenol **3** into the benzyl ether **4** (Scheme 2). The usual method of reacting aryl alcohol **3** with benzyl bromide in the presence of either potassium carbonate or sodium hydride failed to produce benzyl ether **4**, so *Science of Synthesis* was consulted to find alternative methods. The subchapter covering the synthesis of benzyl ethers was quickly identified through the easy to navigate contents page, and it was found that when aryl alcohol **3** was reacted with benzyl bromide in the presence of silver(I) oxide we obtained benzyl ether **4**.

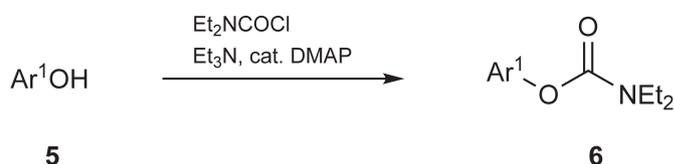
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Scheme 2 Synthesis of Aryl Benzyl Ethers from Aryl Alcohols

Another of our target precursors contained an *O*-aryl carbamate group. Again, the easy to navigate contents page allowed Section 18.6.2.1.4.1, covering the synthesis of carbamates from carbamoyl chlorides, to be quickly located. Using the conditions described for a related example, the phenol **5** was converted to carbamate **6**.



Scheme 3 Reaction of Carbamoyl Chlorides with Alcohols

During the course of this research, it has also been discovered that *ortho*-substituted aryl benzyl ethers can be converted into benzofuran products under modified reaction conditions. *Science of Synthesis* contains a large chapter on the preparation of benzo[*b*]furans. The section covering the synthesis of benzo[*b*]furans by ring-closure of the furan ring (Section 10.1.1.1) allowed alternative approaches to be quickly identified.

Conclusion

In this case study, a text search of *Science of Synthesis* Online has been used to identify methods of achieving enantioselective or diastereoselective [1,2]-Wittig rearrangement of benzyl ethers. The easy to navigate contents page allowed procedures for the synthesis of benzyl ethers and *O*-aryl carbamates to be quickly located. The large chapter on benzo[*b*]furans provided a comprehensive review of their synthesis.